REMARKS

In response to a Notice of Non-Compliant Amendment mailed August 10, 2007, claim 29 has been amended to insert the correct claim identifier. Applicants submit herewith a revised amendment and response to substitute for the response filed on August 7, 2007. The revised response is amended to insert the correct claim identifier.

The undersigned notes that the Notice was not received by mail at the address of record, but rather was accessed by a review of Private PAIR on September 19, 2007. The due date for response to the Notice was August 10, 2007, and, accordingly, Applicants request a one month extension of time to respond to the Notice.

Applicants believe the claimed invention is patentably distinct and respectfully request allowance of the claims and passage of the application to issuance. If any further discussion of this matter would speed prosecution of this application, the Examiner is invited to call the undersigned at (434) 220-2866.

Claim 32 has been amended to further clarify that the control substance present in the test field interacts with the sample to produce a second photometrically detectable signal, wherein the intensity of the second photometrically detectable signal is a function of the amount of the sample applied to the test field. Support for the amendment to claim 34 is found on page 10, lines 1-6.

The present claims are directed to a test strip, a system comprising that test strip, and a method for detecting and quantitating an analyte present in a sample applied to the test strip. More particularly, the system utilizes a test strip that contains two separate reactive agents: 1) a control substance and 2) a reagent, wherein the control substance reacts with the sample matrix (e.g. the solvent) and the reagent reacts with the analyte to be detected. Upon contact of the sample with the control substance and the analyte, detectable signals will be generated by the control substance and the reagent that are indicative of the respective sample fluid volume and analyte concentration. Thus by measuring the signal produced by the control substance, a determination can be made as to whether a sufficient amount of sample has been applied to the test strip or whether the test strip has been filled with less than the optimal amount (underdosed). In the latter case the amount of analyte signal detected can be adjusted to compensate for the underdosing to allow for an accurate determination of the analyte concentration in the sample.

Applicants acknowledge the Examiner's holding that claims 23-31 are allowed.

Claims 21, 32 and 33 stand rejected as being anticipated by Moorman (US Patent No. 5,356,782). Applicants respectfully traverse this rejection.

Moorman discloses the use of a capillary fill device that comprises a negative control, a positive control and reagents for detecting an analyte. However, the reference fails to provide any reagents for detecting the total amount (i.e., volume) of the sample applied to the test field. The Examiner makes reference to the Moorman device as being able to perform a "concentration assay" using an assay based on fluorescence. Yet the disclosed fluorescence detection only relates to detection of the analyte and does not directly measure the volume of the sample added to the test strip. The concentration of the analyte is based on the total amount of analyte detected assuming that the test field was adequately filled. The Moorman device fails to disclose a device that has a separate reagent that interacts with the sample matrix (i.e., the solvent) to indicate the volume of sample that is added to the test strip.

As noted above the present invention advantageously allows the independent measurement of both the total volume of sample present in the test field as well as the amount of analyte present in the test field. This is accomplished through the use of two separate reactive agents. The Moorman device simply does not contain two such separate reactive agents and therefore Moorman fails to anticipate the present invention. Accordingly, applicants respectfully request the withdrawal of the rejection of claims 21, 32 and 33 for anticipation over Moorman.

Claims 32, 33 and 35 stand rejected as being anticipated by Fleming et al (US Patent No. 6,365,417). Applicants respectfully traverse this rejection.

Fleming et al discloses a method for determining when an adequate amount of sample is added to their device. As noted by the Examiner, the passage at column 9, lines 44-47 of Fleming discloses the use of a dye (a "sufficiency indicator") to indicate when sufficient liquid has been collected by the device:

> As saliva moves into and through collection member 80, indicator dye 102 is solubilized and moved along collection member until it reaches indicator window 46. The collection device has been pre-calibrated such that arrival of dye 102 in window 46 signals that sufficient liquid has been collected to perform the analytical tests for which device 20 is designed.

Unlike applicant's device, the "sufficiency indicator" of Fleming does not interact with the sample matrix to "causes a second photometrically detectable signal to be produced

when the test field is illuminated with light" wherein "the intensity of the second photometrically detectable signal is a function of the amount of the sample applied to the test field". In Fleming, the location of a passive dye indicates whether the device has been sufficiently loaded. Accordingly, the Fleming device is incapable of indicating to what extent the device is underdosed, it is only capable of indicating that the device is "full" or "not full". Thus the Fleming device is incapable of adjusting the detected analyte levels when the device is underdosed.

The Examiner notes that Fleming also discusses the detection of photometically detectable signals from their device. Again, similar to Moorman, Fleming only teaches such techniques as "labels" for use in detecting the analyte, not for measuring the amount (volume) of sample added to the device. Furthermore, Fleming is devoid of any teaching or suggestion that it would be advantageous for their "sufficiency indicator" to provide a signal that is proportional to the volume of the sample added to the device. Fleming simply fails to provide any teaching or guidance of how to detect the total volume of a sample applied to the device based on a photometically detectable label.

To further emphasize the difference between the present invention and the device of Fleming applicants have amended claim 32 to state that the intensity of the second photometrically detectable signal is a function of the amount of the sample applied to the test field. The Fleming device is only capable of indicating when a sufficient amount of sample has been added to move the passive dye from a first location to a second location, and fails teach or suggest that the volume of the sample added to the test strip could be measured photometrically based on the interaction between the sample and a control substance present on the test strip.

Accordingly, the Fleming fails to teach a device that comprises two separate reactive agents: 1) a control substance and 2) a reagent, wherein the control substance interacts with the sample matrix (e.g. the solvent) to produce a signal proportional to the volume of sample (when the test field is illuminated with light), and the reagent reacts with the analyte to be detected. Accordingly, Fleming fails to anticipate the present invention and applications respectfully request the withdrawal of the rejection of claim 32, 33 and 35 as being anticipated by that reference.

Claims 19, 22 and 38 stand rejected under 35 USC 103 as being obvious over Moorman in view of Polito et al (US Patent No: 6,136,610). Applicants respectfully traverse this rejection.

The deficiencies of the Moorman disclosure regarding its failure to teach a device that is capable of independently measuring both the volume of sample added to the device as well as the amount of analyte present has been discussed above. The secondary Polito reference fails to supplement the inadequacies of the Moorman teaching with regards to the presence to two separate reactive agents on the device for measuring total sample volume loaded and the amount of analyte present, respectively.

The Examiner contends that the cited Polito reference teaches the use of internal controls for compensating for variations pertaining to the test strip. Thus, the Examiner concludes that it would be obvious to use such controls in the device of Moorman to correct the analyte content in cases of underdosage of the test strip. However, applicants respectfully submit that the internal controls disclosed by Polito are incapable of detecting, or correcting for, underdosaging of test strips. Polito simply discloses the use of a positive control as a means of normalizing the data obtained from two or more separate test strips by comparing the relative signals of the positive control signal from each of the different test strips. Such positive controls do not provide a direct correlation with regards to whether underdosage has occurred, since many different factors may impact the signal strength of the positive internal control, and thus any detected variability between the internal controls can not be definitively assigned to underdosage errors. Furthermore, the internal controls will not compensate for underdosage error when the test strips to be compared are each underdosed. For example, assuming all other parameters were the same between two samples but both samples were applied to the test strip in suboptimal amounts (e.g., each underdosed by 50%) the internal positive controls would give the same reading for each sample and the underdosage of the sample would not be detected.

Claim 19 requires the correction of the analyte content if the amount of sample added to the test element is suboptimal. The internal control components of Polito do not address this issue and only relate to overall normalization of analyte values between two or more test strips. Advantageously, applicants' use of two separate and distinct reactive agents allows for the correction of an underdosed test element based on the readings obtained from a single test element. Applicants were the first to describe the use of a reactive agent in an analyte detection

device that measures the relative amount of the sample matrix (solvent) added to the device based on an interaction between the solvent and the "control substance". The signal produced by the "control substance" is proportional to the amount of sample added to the device, thus allowing for the correction of analyte concentration with underdosage occurs. There is simply no teaching or suggestion in any of the cited references that a second reactive agent (the "control substance") could be added to a test element (in addition to the reactive agent for detecting the analyte) wherein the second reactive agent reacts with the sample matrix to produce a signal proportional to the volume of sample (when the test field is illuminated with light). Nor do any of the cited references suggest how such a measurement of sample volume could be conducted without interfering with the detection of the analyte present in the sample.

Applicants have successfully combined a reagent for detecting and quantitating an analyte with a control substance that measures the amount of sample matrix loaded into a single test element that now allows for both the detection of, and correction of, underdosed test elements. The cited references for all their combined teachings fail to teach or suggest the claimed invention. Accordingly, applications respectfully request the withdrawal of the rejection of claims 19, 22 and 38 as being obvious over Moorman in view of Polito.

Claim 34 stands rejected under 35 USC 103 as being obvious over Moorman in view of Carr et al. Applicants respectfully traverse this rejection.

The deficiencies of the Moorman disclosure regarding its failure to teach a device that is capable of independently measuring both the volume of sample added to the device as well as the amount of analyte present has been discussed above. The secondary Carr reference fails to supplement the inadequacies of the Moorman. As noted by the Examiner Carr discloses that chromophores can be used as labels for "quantification of the products of a synthesis..." including the concentration of a substrate molecule (see page 7, lines 23-30). However the reference is devoid of any suggestion that a chromophore could be used to quantitate the total amount (volume) of liquid that is placed on a test element. Accordingly, both the Moorman and Carr reference fail to teach or suggest the present invention which includes two separate reactive agents, one for detecting the amount of analyte present and the second for detecting the amount of sample present. Accordingly, claim 34 is believed to be patentable over the teaching of Moorman in view of Carr and applicants respectfully request the withdrawal of that rejection.

Claim 35 stands rejected under 35 USC 103 as being obvious over Moorman in view of Caspers et al. Applicants respectfully traverse this rejection.

The deficiencies of the Moorman disclosure regarding its failure to teach a device that is capable of independently measuring both the volume of sample added to the device as well as the amount of analyte present has been discussed above. The secondary Caspers reference fails to supplement the inadequacies of the Moorman. As noted by the Examiner Caspers discloses that a fluorescein dye solution can be used as a low-loss signal coupler in conjunction with fiber optics. The reference while noting that fluorescein can be detected at very low concentrations, fails to suggest that it could be used as a control substance to determine the amount of sample that is placed in contact with the control substance. Accordingly, the reference is devoid of any suggestion that fluorescein could be used to quantitate the amount (volume) of liquid that is placed on a test element. Therefore, the Caspers reference fails to supplement the inadequacies of the Moorman teaching with regards to the present invention. Claim 35 is believed to be patentable over the teaching of Moorman in view of Caspers and applicants respectfully request the withdrawal of that rejection.

Claim 36 stands rejected under 35 USC 103 as being obvious over Moorman in view of Mach et al. Applicants respectfully traverse this rejection.

The deficiencies of the Moorman disclosure regarding its failure to teach a device that is capable of independently measuring both the volume of sample added to the device as well as the amount of analyte present has been discussed above. The secondary Mach reference fails to supplement the inadequacies of the Moorman. Mach discloses that a chlorophenol red dye solution can be used to determine the presence of bacteria. Applicants do not contend that chlorophenol red is a novel dye. However applicants are the first to use this compound in combination with the claimed system and method to measure the amount of liquid added to the test element. Mach is simply devoid of any suggestion that chlorophenol red could be used to quantitate the amount (volume) of liquid that is placed on a test element. Therefore, the Mach reference fails to supplement the inadequacies of the Moorman teaching with regards to the present invention. Claim 36 is believed to be patentable over the teaching of Moorman in view of Mach and applicants respectfully request the withdrawal of that rejection.

Claim 37 stands rejected under 35 USC 103 as being obvious over Moorman in view of Mach et al., as applied to claim 36 and further in view of applicants' admitted prior art on page 15 of the specification. Applicants respectfully traverse this rejection.

The deficiencies of the Moorman disclosure regarding its failure to teach a device that is capable of independently measuring both the volume of sample added to the device as well as the amount of analyte present has been discussed above. The secondary Mach reference fails to supplement the inadequacies of the Moorman. As described above the mere fact that various dyes have been previously disclosed as being useful as labeling reagents does not teach or suggest that such dyes could be used to detect and quantitate the volume of a solution. Applicants do not contend that phosphomolybdic acid is a novel compound. However applicants are the first to use this compound in combination with the claimed system and method to measure the amount of liquid added to the test element. Mach is simply devoid of any suggestion that phosphomolybdic acid could be used to quantitate the amount (volume) of liquid that is placed on a test element. Therefore, the Mach reference fails to supplement the inadequacies of the Moorman teaching with regards to the present invention. Claim 37 is believed to be patentable over the teaching of Moorman in view of Mach and applicants respectfully request the withdrawal of that rejection.

Respectfully submitted,

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